201-14888B

**Substance Group:** **Phenol, Heptyl Derivatives**

**Summary prepared by:** **Petroleum Additives Panel**
**Health & Environmental Research Task Group**

**Date:** **December 2003**

## 1. Physicochemical properties

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## 1.0 Octanol/Water Partition Coefficient

**Robust Summary 28-Octanol-1**

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| CAS No. | 72624-02-3 |
| Test Substance Name | Phenol, heptyl derivatives |
| Method/Guideline | n-Octanol/Water Partition Coefficient, OECD Method 117 |
| GLP (Y/N) | *Not Specified* |
| Year (Published) | 1998 |
| Remarks for Test Conditions | Method involved high performance liquid chromatographic (HPLC) correlation analysis using a reverse phase column. The mobile phase consisted of 70% methanol/30% distilled water with a flow of 1 mL/minute at ambient temperature. Reference materials included: 2-ethylphenol, 2-npropylphenol, naphthalene, biphenyl, phenanthrene and fluoranthenc. The reference and test material were dissolved in methanol (0.1-0.3 mg/mL) and duplicate (5 uL) aliquots were applied to the column. The effluent was monitored at 254 and 270 nm. All reference materials and the test substance had a purity of at least 97%. A calibration curve was prepared on the basis of published $K_{ow}$ values for the reference materials and their retention in the HPLC column, expressed as the capacity factor (k) according to the OECD Guideline. |
| Results | The HPLC correlation analysis revealed that the test material is moderately hydrophobic with a log $K_{ow}$ of 4.5. |
| Conclusions | The n-octanol/water partition coefficient (log $K_{ow}$) was 4.5. |
| Data Quality | Reliable without restriction (Klimisch Code) |
| References | Environmental Toxicology and Chemistry, Volume 17, No. 4, 740-746 (1998). |
| Prepared | September 5, 2003 |

## 2. Environmental Fate and Pathways

## 2.0 Biodegradation

**Robust Summary 28-Biodeg-1**

| ***Test Substance*** | |
|---|---|
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | 100% active ingredient |
| **Method** | |
| Method/Guideline Followed | OECD 301B, Ready Biodegradability, Modified Sturm Test; ASTM D 5864-95 |
| Test Type (aerobic/anaerobic) | Aerobic |
| GLP (Y/N) | Y |
| Year (study performed) | 1997 |
| Contact time (units) | 28 days |
| Test apparatus | *Glass 4-liter Erlenmeyer flasks* |
| Inoculum | Activated sewage sludge from a domestic wastewater treatment plant prepared with soil filtrate per test guideline. Three cultures/group were prepared. The final combined volume of test medium, test substance and inoculum in each test container was 3 liters. Solutions were continuously aerated with $CO_2$ free air. The test substance was incrementally added at concentrations of 4, 8 and 8 mg C/L on days 0, 7 and 11. On day 14 equal volumes of each culture were combined and the composite inoculum screened and homogenized. A standard plate count was performed on the inoculum. Plates were incubated at 20±3°C for approximately 48 hours. |
| Cultures/replicates: | *Three replicate test cultures, three replicate blank control cultures and three reference control cultures.* |
| Temperature of incubation: | 20±3°C |
| Dosing procedure: | Neat test chemical was gravimetrically added to glass cover slips, which were then added to culture medium in test vessels. |
| Study initiation: | Test flasks provided with $CO_2$ free air and mixed with a magnetic stirrer. The $CO_2$ produced from the degradation of organic carbon sources within each test chamber was trapped as $K_2CO_3$ in 0.5 N KOH and measured using a carbon analyzer. |
| Sampling: | Days 2, 5, 11, 13, 16, 18, 23 and 29 (after acidification on day 28) |
| Concentration of test substance: | 10 mg C/L weighed directly onto tared glass slides and placed into each test substance flask. |
| Controls: | Blank and positive controls used per guideline. Positive control was canola oil added to control vessels at a loading of 10 mg C/L. |
| Analytical method: | The $CO_2$ produced from the degradation of organic carbon sources within each test chamber was trapped as $K_2CO_3$ in 0.5 N KOH and measured using a carbon analyzer. |

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| Study termination: | On day 28 the pH of the content of each test flask was determined. The flasks were then acidified with 3 ml of concentrated hydrochloric acid to drive off inorganic carbonate. The chambers were aerated overnight and then the trapping solutions closest to the test chambers were analyzed for inorganic carbon. |
| Method of calculating biodegradation values: | Percent biodegradation calculated as percent ratio of cumulative net carbon dioxide to theoretical carbon dioxide as determined from elemental analysis of the test material. |
| ***Results*** | The test substance was not considered readily biodegradable under the criteria that requires 60% biodegradation within 28 days, achieved within 10 days of reaching 10% biodegradation. The $CO_2$ production from the reference chemical exceeded the 60% of theoretical necessary to consider the test valid. |
| Degradation % | Test substance: 25.4 $\pm$ 1.4 % in 29days (average final pH 7.1)<br>Positive control substance: 91.5 $\pm$ 0.8 % in 29 days |
| ***Conclusions*** | The test substance was not readily biodegradable. |
| ***Data Quality*** | Reliable without restriction. (Klimisch Code) |
| ***References*** | Confidential business information |
| ***Other*** | Updated: 5/27/2003 |

## AQUATIC ORGANISMS

## 3.0 Acute and Prolonged Toxicity to Fish

**Robust Summary 28-Fish-1**

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|---|---|
| Test Substance | |
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | Minimum of 97% |
| Method | |
| Method/Guideline followed | Similar to OECD Guideline for Testing of Chemicals #203, Fish Acute Toxicity Test (1984). |
| Test Type | Acute Toxicity to Fish (flow through test conditions) |
| GLP (Y/N) | Not specified |
| Year (Study Published) | 1998 |
| Species/Strain | Atlantic Cod |
| Fish Number | 21/concentration (7/replicate) |
| Fish Size | Average weight 1.1 g |
| Analytical Monitoring | Not specified |
| Nominal Test Substance Concentration Levels | Vehicle Control (methanol treated water), 0.5, 1, 2.1 and 4.2 umol/L |
| Test Concentration Preparation | Not Described |
| Exposure Period | 168 hours |
| Exposure Conditions | Flow through test conditions. |
| Vehicle | Methanol |
| Statistical Analysis | ANOVA, Mann-Whitney U test |
| Dose Rangefinding Study | No |
| Test Chambers | 1.5-liter glass aquaria |
| Diluent Water | Temperature: 9.7 $^{o}$C<br>Salinity: 32.7<br>Oxygen Saturation: 89%<br>pH: 8.1 |
| Photoperiod | 12-h light per day, 50 Lux. |
| Positive Control | No |
| Remarks field for test conditions | Pretreatment: none, fish held for a minimum of 14 days before testing. No feeding 24 hours prior to and during the test. All organisms were observed for mortality twice daily |
| Results | Cumulative mortality (%) was as follows: |

| | % Cumulative Mortality (n=21) | | | | | | |
|---|---|---|---|---|---|---|---|
| Nominal Concentration (umol/L) | 0 hours | 48 hours | 72 hours | 96 hours | 120 hours | 144 hours | 168 hours |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 0 | 0 | 5 | 5 | 5 | 5 | 2 |

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| | 1 0 0 0 0 0 0 0<br>2.1 0 0 0 10* 10* 14* 19*<br>4.2 0 5 67* 100* - - -<br>*=Significantly different from control p≤0.05.<br><br>The maximum nominal concentration causing no mortality was 1.0 umol/L. The minimum concentration causing 100% mortality was 4.2 umol/L. The 96 hr LC50 was estimated by graphical interpolation to be 2.9 umol/L. No mortality was observed in the vehicle control (methanol/water) group. |
| Conclusions | The 96 hr LC50 was 2.9 umol/L. The 96 hour NOEC was 1 umol//L. |
| Data Quality | Reliable with restriction (Klimisch Code). Restriction due to lack of analytical confirmation of test material concentration. |
| References | Environmental Toxicology and Chemistry, Volume 17, No. 4, 740-746 (1998). |
| Other | Updated: September 5, 2003 |
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## 4. Toxicity

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### 4.1 Acute Toxicity

#### 4.1.1 Acute Oral Toxicity

**Robust Summary 28-Acute Oral –1**

| ***Test Substance*** | |
|---|---|
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | 100% active ingredient |
| **Method** | |
| Method/Guideline followed | Similar to FHSA 16 CFR 1500.3 |
| Test Type | Acute oral toxicity |
| GLP (Y/N) | Y |
| Year (Study Performed) | 1982 |
| Species/Strain | Rats/Sprague-Dawley strain |
| Sex | Male and Female |
| No. of animals/dose | 5/sex |
| Vehicle | None |
| Route of administration | Oral (intragastric) |
| Dose level | 2.0 g/kg |
| Dose volume | Not provided |
| Control group included | No |
| Remarks field for test conditions | A single dose of the undiluted test material was administered intragastrically to five fasted (over night) male and female rats. The animals were observed for signs of toxicity or behavioral changes frequently on the day of dosing and twice daily thereafter. Individual weights were recorded on the day of dosing. Gross autopsies were performed on all animals. |
| ***Results*** | LD50 <2.0 g/kg (males and females) |
| Remarks | Four of five females died within 24 hours post dosing. The remaining female and all of the males died on days 2 and 3. The animals were ruffled after 3 hours. They had dirty oily coats, appeared depressed and had discharge around the mouth and nose after 24 hours. All animals died prior to the first post dosing weighing interval. At necropsy pale and mottled livers and pale spleens were observed. |

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| ***Conclusions*** | The test article, when administered as received to male and female Sprague-Dawley rats, had an acute oral LD50 of <2.0 g/kg (males and females.). |
| ***Data Quality*** | Reliable with restriction (Klimisch Code). Restriction due to the lack of individual animal data in the final report. |
| ***References*** | Unpublished confidential business information |
| ***Other*** | Updated: 5/30/2003 |
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**Robust Summary 28-Acute Oral –1**

| ***Test Substance*** | |
|---|---|
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | 100% active ingredient |
| **Method** | |
| Method/Guideline followed | Similar to FHSA 16 CFR 1500.3 |
| Test Type | Acute oral toxicity |
| GLP (Y/N) | Y |
| Year (Study Performed) | 1982 |
| Species/Strain | Rats/Sprague-Dawley strain |
| Sex | Male and Female |
| No. of animals/dose | 5/sex |
| Vehicle | None |
| Route of administration | Oral (intragastric) |
| Dose level | 0.2 g/kg |
| Dose volume | Not provided |
| Control group included | No |
| Remarks field for test conditions | A single dose of the undiluted test material was administered intragastrically to five fasted (over night) male and female rats. The animals were observed for signs of toxicity or behavioral changes frequently on the day of dosing and twice daily thereafter. Individual weights were recorded on the day of dosing, on day 7 and at termination. All animals were euthanized at the conclusion of the observation period. Gross autopsies were performed on all animals after 14 days. |
| ***Results*** | LD50 >0.2 g/kg (males and females) |
| Remarks | All animals survived the duration of the study. The animals were ruffled after 3 hours. They had dirty coats with urine stains and a bloody discharge around the nose and mouth within 24 hours. Between 12 and 24 hours the animals were vocalizing. The dirty coats and discharge gradually improved and the animals appeared to be recovered by day 3. The males exhibited an 8% decrease in mean body weight during week 1. Male body weights recovered during week 2. Female body weights were unremarkable. Necropsy results were unremarkable. |
| ***Conclusions*** | The test article, when administered as received to male and female Sprague-Dawley rats, had an acute oral LD50 of >0.2 g/kg (males and females.). |
| ***Data Quality*** | Reliable with restriction (Klimisch Code). Restriction due to the lack of individual animal data in the final report. |
| ***References*** | Unpublished confidential business information |
| ***Other*** | Updated: 5/30/2003 |
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## 4.1.2 Acute Dermal Toxicity

| ***Test Substance*** | |
|---|---|
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | 100% active ingredient |
| **Method** | |
| Method/Guideline followed | OECD Guideline 402 and EPA Pesticide Assessment Guidelines (November 1982) |
| Test Type | Acute dermal toxicity (Limit Test) |
| GLP (Y/N) | Yes |
| Year (Study Performed) | 1985 |
| Species/Strain | Rabbits/New Zealand White |
| Sex | Male and female |
| No. of animals/sex/group | 5 |
| Vehicle | None |
| Route of administration | Dermal |
| Dose level | 2 g/kg |
| Control group included | No |
| Remarks field for test conditions | Approximately 24 hours prior to topical application of the test material, the hair of each animal was closely clipped. A single dose of 2 g/kg of the undiluted test material was administered dermally to five male and five female animals. The test material was kept in contact with the skin for a period of 24 consecutive hours under a gauze pad and wrapped with an impervious material. The application site was washed clean of residual test material at the end of the 24-hour exposure period. The animals were observed for abnormal clinical signs once or twice/day for 14 days after treatment. Individual body weights were recorded on the day of dosing, weekly thereafter and prior to sacrifice. Gross necropsies were performed on all animals on Day 14. |
| ***Results*** | LD50 > 2.0 g/kg (males and females) |
| Remarks | No male mortality was observed. One female animal was found dead on day 12. This female exhibited a body weight loss at day 7 as well as diarrhea, signs of dehydration and a lack of formed fecal material in the lower gastrointestinal tract at necropsy.<br><br>In the males signs of necrosis and severe edema were observed in 5 of 5 animals after unwrapping at 24 hours. Eschar was noted at 48 hours (3/5) and 72 hours (2/5). The eschar began to peel at 7 days. One male exhibited a loss of body weight at 7 and 14 days.<br><br>In the females signs of necrosis and severe edema were observed in 5 of 5 animals after unwrapping at 24 hours. Eschar was noted at 48 hours (5/5). The eschar began to peel at 8 days. No gross necropsy findings were evident in the males or females that were sacrificed on day 14. |

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| ***Conclusions*** | The test article, when administered dermally as received to 5 male and 5 female New Zealand white rabbits had an acute dermal LD50 of greater than 2.0 g/kg. |
| ***Data Quality*** | Reliable without restriction (Klimisch Code). |
| ***References*** | Unpublished confidential business information |
| ***Other*** | Updated: 5/29/2003 |
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## 4.2 Genetic Toxicity:

**Robust Summary 28-Gentox:-1**

| ***Test Substance*** | |
|---|---|
| CAS # | CAS# 72624-02-3 |
| Chemical Name | Phenol, heptyl derivatives |
| Remarks | 100% active ingredient |
| **Method** | |
| Method/Guideline followed | OECD Guideline 471 |
| Test Type | Bacterial Reverse Mutation Assay |
| GLP (Y/N) | Y |
| Year (Study Performed) | 1993 |
| Test System | *Salmonella typhimurium* and *Escherichia Coli* |
| Strains Tested | *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537; TA1538 *Escherichia Coli* tester strain WP2*uvr*A |
| Exposure Method | Plate incorporation |
| Test Substance Doses/concentration levels | Initial assay:<br>All *Salmonella* Strains + (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate<br>All *Salmonella* Strains - (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate<br>WP2*uvr*A + (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate<br>WP2*uvr*A - (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate<br>Confirmatory Assay A:<br>TA1538 + (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate<br>TA1535, 1537, 98, 100 and WP2*uvr*A + (S9): 1.67, 5.0, 16.7, 50, 167 and 500 ug/plate<br>All *Salmonella* Strains - (S9): 0.05, 0.167, 0.5, 1.67, 5.0 and 16.7 ug/plate<br>WP2*uvr*A - (S9): 0.167, 0.5, 1.67, 5.0, 16.7, and 50 ug/plate<br>Confirmatory Assay B:<br>TA1535, 1537, 98 and 100 + (S9): 0.5, 1.67, 5.0, 16.7, 50 and 100 ug/plate<br>WP2*uvr*A + (S9): 0.167, 0.5, 1.67, 5.0, 16.7, 50 and 100ug/plate |
| Metabolic Activation | With and without (6% S9 fraction mix of livers of Aroclor 1254 pretreated Sprague Dawley rats) |
| Vehicle | DMSO |
| Tester strain, activation status, Positive Controls and concentration level | TA98 +S9 2-anthramine 2.5 ug/plate<br>TA98 -S9 2-nitroflourene 5.0 ug/plate<br>TA100 +S9 2-anthramine 2.5 ug/plate<br>TA100 -S9 sodium azide 10.0 ug/plate<br>TA1535 +S9 2-anthramine 2.5 ug/plate<br>TA1535 -S9 sodium azide 10.0 ug/plate<br>TA1537 +S9 2-anthramine 2.5 ug/plate<br>TA1537 -S9 9-aminoacridine 150.0 ug/plate<br>TA1538 +S9 2-anthramine 2.5 ug/plate<br>TA1538 -S9 2-nitroflourene 5.0 ug/plate<br>WP2*uvr*A +S9 2-anthramine 2.5 ug/plate<br>WP2*uvr*A –S9 ENNG 2.0 ug/plate |
| Vehicle Control | DMSO |

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| Statistical Analysis | Mean revertant colony count and standard deviation were determined for each dose point. Statistical analysis was performed as appropriate. |
| Dose Rangefinding Study | Conducted using tester strains TA1538, TA100 and WP2*uvr*A and ten doses of test material ranging from 0.5to 5,000 ug/plate, duplicate plates/dose without metabolic activation. Cytotoxicity was evaluated. |
| S9 Optimization Study | Yes |
| Remarks field for test conditions | In the main study there were two treatment sets for each tester strain, with (+S9) and without (-S9) metabolic activation. Each of the tester strains was dosed with several concentrations of test substance, vehicle controls, and a positive control. Three plates/dose group/strain/treatment set were evaluated. The results of the initial assay were confirmed in two independent confirmatory experiments. 0.1 mL of test material, positive control or vehicle control were added to each plate along with 0.1 mL of tester strain, S9 mix (if needed) and 2.0 mL of top agar. This was overlaid onto the surface of minimal bottom agar in a petri dish. Plates were incubated for 48 hours at 37$^{o}$C. The condition of the bacterial background lawn was evaluated for cytotoxicity and test article precipitate. Revertant colonies were counted using an electronic colony counter. A positive result was defined as a statistically significant dose dependent increase in the number of revertants with at least one dose level inducing a revertant frequency that is two-fold the level of the solvent control. |
| ***Results*** | The test substance was not mutagenic in this assay with or without metabolic activation. |
| Remarks | The test material was evaluated in a toxicity prescreen in strains TA1538, TA100 and WP2*uvr*A. Results of this evaluation indicated that the test material produced inhibited growth or complete toxicity in all three tester strains at all dose levels tested (50-5000 ug/plate). The dose range find study was repeated at doses ranging from 0.5 to 167 ug/plate. Doses > 5 ug/plate were toxic in TA1538 and TA100 and in doses > 16.7 ug/plate in WP2*uvr*A. Based on these results the mutagenicity assay was conducted at the concentrations listed above. The test material was soluble at all concentrations tested.<br><br>In the mutagenicity study, inhibited growth was observed in all tester strains at doses between 0.5 and 16.7 and/or 50 ug/plate with S9, and in TA1538 at 5 and 16.7 ug/plate without S9. Revertant frequencies at all dose levels in all tester strains with and without metabolic activation were less than those observed in the concurrent negative controls.<br><br>The test material was re-evaluated in a confirmatory assay in all tester strains activation at the confirmatory dose levels listed above (Confirmatory Assay A). The test material was soluble at all concentrations tested. Inhibited growth was observed in all tester strains at the highest two or three concentrations tested with and without metabolic activation. Revertant frequencies at all five dose levels in all *Salmonella* tester strains with metabolic activation, and in all six tester strains without activation, approximated or were less than those observed in the concurrent negative controls. A statistically significant, 2.6 fold increase was observed in the revertant frequency of WP2*uvr*A at 1.67 ug/plate. This increase was not dose related.<br><br>**Based on these confirmatory assay results a second confirmatory assay** (Confirmatory Assay B) was conducted. The test article was freely soluble and inhibited growth was observed in all tester strains at 16.7 and 50 and/or 100 ug/plate with activation. A statistically significant, 2.1 fold increase was observed in the revertant frequency of TA1537 at 16.7 ug/plate. This increase was not dose related. The Study Director considered the slight increases observed in the revertant frequencies of TA1537 and |

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| | WP2*uvr*A to be random fluctuations of the revertant frequencies.<br>The positive and negative controls for each respective test strain were within acceptable limits. |
| ***Conclusions*** | Under the conditions of this study, the test material was not mutagenic. |
| ***Data Quality*** | Reliable without restriction (Klimisch Code) |
| ***References*** | Unpublished confidential business information |
| ***Other*** | Updated: 7/17/2003 |
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